

**Task History**

June 22, 2011 10:26 PM

**Saved answer set '10581274' opened**

Answer set 6 created with 2 reference answers from CAPLUS

**Detailed display from Answer set 6 of Highly Potent, Orally Available Anti-inflammatory Broad-Spectrum Chemokine Inhibitors**

# Highly Potent, Orally Available Anti-inflammatory Broad-Spectrum Chemokine Inhibitors

By: Fox, David J.; Reckless, Jill; Lingard, Hannah; Warren, Stuart; Grainger, David J.

A series of 3-acylaminocaprolactams are inhibitors of chemokine-induced chemotaxis. Branching of the side chain  $\alpha$ -carbon provides highly potent inhibitors of a range of CC and CXC chemokines. The most potent compd. has an ED50 of 40 pM. Selected compds. were tested in an in vivo inflammatory assay, and the best compd. reduces TNF- $\alpha$  levels with an ED50 of 0.1  $\mu$ g/kg when administered by either s.c. injection or oral delivery.

## Indexing

Pharmacology (Section 1-3)

## Concepts

Anti-inflammatory agents  
Cell migration  
Chemotaxis  
Human  
Inflammation  
Neutrophil  
Structure-activity relationship  
oral antiinflammatory broad-spectrum chemokine inhibitors

CC chemokines  
CXC chemokines  
Chemokines  
Interleukin 8  
Macrophage inflammatory protein 1 $\alpha$   
Monocyte chemoattractant protein-1  
RANTES(chemokine)  
Tumor necrosis factors  
oral antiinflammatory broad-spectrum chemokine inhibitors  
Biological study, unclassified; Biological study

## Source

Journal of Medicinal Chemistry  
Volume 52  
Issue 11  
Pages 3591-3595  
Journal  
2009  
CODEN: JMCMAR  
ISSN: 0022-2623  
DOI:  
10.1021/jm900133w

## Company/Organization

Department of Chemistry  
University of Cambridge  
Cambridge, UK CB2 1EW

## Accession Number

2009:565761  
CAN 151:23962  
CAPLUS

## Publisher

American Chemical Society

## Language

English

## Substances

853905-44-9P  
oral antiinflammatory broad-spectrum chemokine inhibitors  
Drug mechanism of action; Pharmacological activity; Reactant; Synthetic preparation; Therapeutic use;  
Biological study; Preparation; Uses; Reactant or reagent

726187-67-3P  
853905-34-7P  
853905-39-2P  
853905-40-5P  
853905-41-6P  
853905-42-7P  
853905-45-0P  
853905-59-6P  
853905-60-9P  
853905-61-0P  
853905-62-1P  
853905-68-7P  
853905-72-3P  
876063-97-7P  
876063-98-8P  
876063-99-9P  
876064-01-6P  
876064-02-7P  
876064-03-8P  
1160115-32-1P  
1160115-34-3P

oral antiinflammatory broad-spectrum chemokine inhibitors

Drug mechanism of action; Pharmacological activity; Synthetic preparation; Therapeutic use; Biological study; Preparation; Uses

108-18-9 Diisopropylamine  
112-31-2 Decanal  
547-63-7 Methyl isobutyrate  
671-42-1  
870-63-3  
924-50-5 Methyl 3,3-dimethylacrylate  
2094-72-6 1-Adamantanecarbonyl chloride  
2719-27-9 Cyclohexanecarbonyl chloride  
2890-61-1 1-Methylcyclohexanecarbonyl chloride  
3282-30-2 2,2-Dimethylpropionyl chloride  
4301-04-6  
5856-77-9 2,2-Dimethylbutyryl chloride  
15721-22-9 2,2-Dimethylpentanoyl chloride  
19835-38-2  
21568-87-6  
26081-07-2  
28957-33-7  
36278-22-5 1-Cyclohexenecarbonyl chloride  
39482-46-7 2,2-Dimethyl-4-pentenoyl chloride  
39691-62-8 Nonylmagnesium bromide  
50321-59-0  
60631-34-7 2,2-Dimethyldodecanoyl chloride  
67589-90-6  
73152-73-6  
oral antiinflammatory broad-spectrum chemokine inhibitors  
Reactant; Reactant or reagent

2198-82-5P 2,2,5-Trimethyl-4-hexenoic acid  
53663-29-9P (E)-2-Methyldodec-2-enoic acid  
66478-19-1P  
102944-03-6P 3,3-Dimethyldodecanoic acid  
476690-74-3P (E)-Ethyl 2-methyldodec-2-enoate  
853905-71-2P  
1017249-22-7P  
1017249-74-9P

oral antiinflammatory broad-spectrum chemokine inhibitors

Reactant; Synthetic preparation; Preparation; Reactant or reagent

### Supplementary Terms

oral antiinflammatory chemokine inhibitor structure

### Citations

- 1a) Gerard, C; *Nat Immunol* 2001, 2, 108
- 1b) Horuk, R; *Cytokine Growth Factor Rev* 2001, 12, 313
- 1c) Rollins, B; *Blood* 1997, 90, 909
- 1d) Luster, A; *N Engl J Med* 1998, 338, 436
- 1e) Thelen, M; *Nat Immunol* 2001, 2, 129
- 2) Viola, A; *Annu Rev Pharmacol Toxicol* 2008, 48, 171
- 3a) Ribeiro, S; *Pharmacol Ther* 2005, 107, 44
- 3b) Carter, P; *Curr Opin Chem Biol* 2002, 6, 510
- 3c) Allen, S; *Annu Rev Immunol* 2007, 26, 787
- 4a) Vaidehi, N; *J Biol Chem* 2006, 281, 27613
- 4b) Pasternak, A; *Bioorg Med Chem Lett* 2008, 18, 1374
- 4c) Santella, L; *Bioorg Med Chem Lett* 2008, 18, 576
- 4d) Thoma, G; *Bioorg Med Chem Lett* 2008, 18, 2000
- 5a) Vandercappellen, J; *Cancer Lett* 2008, 267, 226
- 5b) Biju, P; *Bioorg Med Chem Lett* 2008, 18, 228
- 6a) Reckless, J; *Biochem J* 1999, 340, 803
- 6b) Reckless, J; *Immunology* 2001, 103, 244
- 7a) Fox, D; *J Med Chem* 2002, 45, 360
- 7b) Fox, D; *J Med Chem* 2005, 48, 867
- 8a) Grainger, D; *Biochem Pharmacol* 2003, 65, 1027
- 8b) Naidu, B; *Ann Thorac Surg* 2003, 75, 1118
- 8c) Wilbert, S; *Anal Biochem* 2000, 278, 14
- 9) Schroff, R; *Mini-Rev Med Chem* 2005, 5, 849
- 10) Frow, E; *Med Res Rev* 2004, 24, 276
- 1) Boyle, W; *J Am Chem Soc* 1979, 44, 4841
- 2) Rezler, E; *J Med Chem* 1997, 40, 3508
- 3) Reckless, J; *Biochem J* 1999, 340, 803
- 4) Fox, D; *J Med Chem* 2002, 45, 360
- 5) Fox, D; *J Med Chem* 2005, 48, 867
- 6) Frow, E; *Med Res Rev* 2004, 24, 267

### Tags

0 Tags

### Comments

0 Comments

Copyright © 2011 American Chemical Society (ACS). All Rights Reserved.